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PERNICIOUS ANEMIA

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Before discussing the subject of anemia, perhaps it would be well to go over a little of the normal physiology of the blood and blood-forming organs. The blood is a red, slightly alkaline fluid that is pumped by the heart into the arteries, thence into the capillaries and back to the heart again by way of the veins. It is a closed circuit very well represented by a Davidson syringe with a piece of rubber tubing attached to both ends, in which the bulb represents the heart and the tubing the arteries, veins and capillaries. It serves to carry oxygen and food to all parts of the body and to return their waste material to be removed by the kidneys and lungs.

In the blood vessels during life the blood consists of a fluid portion called the plasma in which are suspended the red and white blood cells. But when the blood is withdrawn from the body and allowed to stand in a glass vessel, it clots or coagulates so as to form a solid jelly. After some time this jelly or clot begins to shrink and there is squeezed out a clear, yellowish fluid called serum. It is this serum that is used to make many of the biological tests such as the Wassermann, Widal, etc., and this serum, when derived from the horse, contains the anti-toxins now in such common use. The remaining red clot contains the blood cells, enmeshed in a stringy substance called "fibrin." If instead of allowing the blood to stand, it is immediately whipped up with some instrument, much as one would whip an egg with a fork, the fibrin can be removed and the blood will remain a red liquid known as defibrinated blood. The serum will coagulate into a solid mass when heated to 58°C. so one must be careful not to allow curative sera to get too warm during any heating process previous to their administration.

The plasma forms about one half the bulk of the whole of the circulating blood, and the cells form the other half; the whole blood forms about one-thirteenth of the body weight, except in very fat people where it is less.

The red cells are minute, bi-concave discs having by themselves, when examined under the microscope, a pale yellow appearance, but massed together they give a red color. In health their number varies from about 4,500,000 in women to about 5,500,000 (or even 6,000,000) in robust men, to each cubic millimeter, a drop about the size of the head of any ordinary pin ($\frac{1}{75}$ inch cube). About 40 per cent of the red

cell is solid matter, and of this 40 per cent about 90 per cent is haemoglobin, its most important constituent and the substance that carries the oxygen and gives the blood its red color.

Various instruments have been devised for estimating the amount of haemoglobin. The normal, or 100 per cent, is that found in a healthy adult and is determined by comparison with some color scale. A common means of estimating the haemoglobin percentage is to receive a drop of blood on a piece of thin, specially prepared, blotting paper. After drying, this color is compared with ten graded colors lithographed on paper. This Tallquest instrument is not very accurate, but it gives an easy and quick method of determining approximately the degree of anemia.

In order to study the cells, a small drop of blood should be smeared out thinly and evenly on a scrupulously clean glass slide. This smear is allowed to dry in the air and is either "fixed" by heat and subsequently stained, or it is "fixed" and stained at the same time. It is their behaviour toward the anilin dyes that classifies the different cells.

The normal red cell or erythrocyte is about 7.5 micra ($\frac{1}{25,000}$ of an inch) in diameter, has no nucleus and stains by the acid dye, eosin, but not by the basic dye, methylene blue. In the healthy adult this is the only type of red cell seen, but in disease, in addition to this normal cell, one sees large red cells called "megalocytes," small red cells called "microcytes" and irregular pear shaped cells called "poikilocytes. When poikilocytes are seen, the condition of "poikilocytosis" is said to be present, and when there is a great variation in the size of the cells, the condition of "anisocytosis" is said to be present. In disease also there appear nucleated red cells, the nucleus staining deeply with methylene blue and the cell body staining with eosin. When of normal size these cells are called "normoblasts," when large, "megaloblasts," and when very small, "microblasts."

There are about 6000 white cells or leucocytes to each cubic millimeter of blood, and when the number of white cells to each cubic millimeter is increased, the condition of "leucocytosis" is said to be present. In health there are usually five forms or kinds distinguished. The lymphocyte (forming about 25 per cent of all the white cells) is about the size of the red cell or slightly larger, with a nucleus almost as large as the cell itself. It is derived from the lymphoid tissue scattered throughout the body. The large mononuclear cell is about two or three times the size of a red cell and has an eccentric nucleus. They are found in the bone marrow and make up about 4 per cent of the total number of white cells. The polynuclear cell has an irregular "S" or horseshoe-shaped nucleus, is formed in the bone marrow and makes up

about 65 per cent to 75 per cent of the white cells. It is mainly this cell that is increased during any form of blood poisoning or pus formation such as pneumonia, empyema, suppurative appendicitis, peritonitis, etc. The eosinophile cell is like the polynuclear cell except that its cell body contains granules staining deeply with eosin. It makes up about 2 per cent of the total number of white cells. The mast cell, forming about 0.5 per cent of the total number of white cells, is similar to the eosinophile cell, except that the granules are basophilic, staining deeply with methylene blue.

In disease there appear various other forms of white cells, the most important of which are the "myelocytes." They are like the large mononuclear cell, except that the cell body has deeply staining granules.

The estimation of the number of white and red cells is made by the Thoma-Zeis instrument. This consists of a counting chamber, a glass slide to which is cemented a small disc of glass in the center surrounded by a glass square with its central portion cut out in the form of a circle so as to leave a sort of moat between the disc and the square. The level of the accurately-ground glass disc is just $\frac{1}{10}$ millimeter below the level of the glass square, so that when a drop of blood is placed upon the disc and an accurately ground glass cover slip is pressed down upon the outside glass square, the depth of the layer of blood will be exactly $\frac{1}{10}$ of a millimeter. On this central disc are cut some lines, ruled so as to make tiny squares of $\frac{1}{400}$ of a square millimeter. Consequently the layer of fluid covering each tiny square would be $\frac{1}{10}$ by $\frac{1}{400}$ or $\frac{1}{40000}$ of a cubic millimeter. The number of blood cells found in perhaps 100 of these small squares is then counted and averaged for each square, the result multiplied by 4000 gives the number of cells to a cubic millimeter, after a further multiplication to allow for the blood dilution.

The apparatus is completed by two small, accurately-graduated pipettes, in order that the blood may be diluted with a definite amount of fluid, else the cells would be too thick to be countable.

In order to collect the blood the lobe of the ear, after cleansing by alcohol and ether, is pricked with an acne lancet (a Hagedorn needle is the next best instrument) and a good sized drop of blood is allowed to collect. The tip of the pipette is immersed in this drop and the blood is sucked up to the 0.5 mark and then the diluting fluid is sucked up to the 10 mark for red cells and the 11 mark for white cells. It is thoroughly mixed by a small glass bead contained in the mixing chamber.

These three examinations have been described more or less in detail, for it is practically only by the blood examination that a diagnosis of the various blood diseases can be made.

To recapitulate, then, there are three important examinations to be made: First, the estimation of the haemoglobin; second, the counting of the number of red and white cells; third, the examination of the stained blood; fourth, the determination of what is called the color index from the first and second examinations. This is done by calculating the percentage 5,000,000 that our count is, and using this as the denominator of a fraction, the numerator of which is the hæmoglobin percentage. Thus, if the count were 4,000,000, that would be 80 per cent of the normal 5,000,000 and if the haemoglobin percentage were 60 per cent, the fraction would be 60/80 or a color index of 0.75. Had the haemoglobin percentage been 80, the color index would have been 1, and had it been 90 per cent, the color index would have been 1.1, a high color index typical of pernicious anemia.

Not quite so much is known of the blood-forming organs as is known of the blood. It is probable that during foetal life the blood cells may be formed from the endothelial cells lining the blood vessels and that later they are formed in the liver. During adult life the cells, with the exception of the lymphocytes, formed in the lymphoid tissue, are formed in the bone marrow.

Anemia, literally meaning without blood, is present when there is a diminution of either the red cells or the haemoglobin, or of both. Some time ago, before the more common use of the microscope, the only thing that distinguished pernicious anemia from the others was that it was always fatal. Unfortunately that distinguishing characteristic still holds good, but now one can say a case is pernicious anemia some time before death. A very common classification of anemia has been into primary and secondary. In secondary anemia there is always an apparent cause such as cancer, and in primary anemia it has been supposed to be without any other disease condition being present. However, if the blood is looked upon, not as an organ, but as a secretion from other organs, as the gastric juice is a secretion of the stomach, then all anemias would really be secondary, as Vogel suggests. He would classify them into anemias due, first, to a reduced production of blood, and second, an abnormal destruction.

In the first group would be the anemias due to cachexia or the wasting diseases, the aplastic type of pernicious anemia, and the so-called osteosclerotic anemia. In the second group would be the anemias due to hemorrhage and to the poisons like nitro benzol, potassium chlorate, acetanilid, etc., and those due to intestinal worms, malaria, pregnancy, syphilis and cancer, hemolytic jaundice, splenic anemia and the true pernicious anemia.

In all classifications chlorosis is put by itself. This is the peculiar

type seen in young girls when the number of cells may be high but the haemoglobin is markedly reduced.

Then there are the other so-called blood diseases in which there is an anemia but there is also some other distinguishing characteristic: notably, leukaemia of four types—acute and chronic, lymphatic, showing a great increase in the small white cells (the lymphocytes) and the acute and chronic myelogenous, where there is an enormous increase of all of the kinds of white cells but especially of the “myelocytes.”

(To be continued)

HEREDITY AND CONTAGION IN CANCER

The American Society for the Control of Cancer issues a statement on this subject, saying:

Perhaps no aspect of the cancer problem causes such widespread apprehension as the possibility of its being inherited. Broadly speaking such fears are probably groundless. When the disease occurs repeatedly in the same family there is a tendency to assume that it is inherited. This reasoning is of course superficial. Newsholme, Bashford and many other authorities have frequently pointed out that cancer is such a common disease among adults that by the laws of chance alone many cases are likely to occur in some families. It should be remembered that among people over forty years of age in this country cancer causes the death of one woman out of every eight and one man out of every fourteen. It is obvious that repeated instances must occur in some families and this of itself does not prove that cancer is hereditary. Important laboratory studies tend to prove the hereditary transmission of a liability to cancer among mice, but many leading authorities believe that we are not yet justified in applying these deductions to the human subject. Previous statistical investigation among human beings has failed to establish the inheritance of cancer and Mr. Hunter's study merely adds to the mass of evidence against heredity as a causative factor. In passing upon applications, insurance companies generally regard the history of cancer in the family as of little significance. The practical bearings of competent investigations of the human material should be brought home to newspaper readers in an effort to reduce the present excessive apprehension among the people regarding the possibility of inheriting cancer.

With regard to contagion we are on even firmer ground and the question may be regarded as settled. After countless operations there is no case recorded in which a surgeon or nurse has acquired cancer from the treatment or attendance upon any patient suffering from this disease. The public should be taught that the fear of infection is groundless since apprehension on this score has undoubtedly tended in many cases to prevent the most humane care of sufferers from a disease which, especially in its advanced stages, demands the utmost resources of patient and merciful ministration on the part of relatives and nurses.